CLAIMS

We claim:

1. A probe for detection of a disease or condition, the probe being adapted to distinguish between functional $P2X_7$ receptors and non-functional $P2X_7$ receptors.

2. The probe of claim 1, wherein the probe is adapted to distinguish between functional $P2X_7$ receptors and non-functional $P2X_7$ receptors by detecting change in relation to binding of adenosine triphosphate (ATP) to the receptors.

3. The probe of claim 1, wherein the probe is adapted to distinguish between functional $P2X_7$ receptors and non-functional $P2X_7$ receptors by detecting change in binding of one or more proteins necessary for pore formation in $P2X_7$ receptors.

4. The probe of claim 3, wherein the probe is adapted to distinguish between functional $P2X_7$ receptors and non-functional $P2X_7$ receptors by detecting one or more parts of the receptor exposed in the absence of bound ATP.

5. The probe of claim 4, wherein the part includes a $P2X_7$ monomer.

6. The probe of claim 1, which is natural or artificial.

7. The probe of claim 1, wherein the probe is an antibody chosen from the group consisting of a polyclonal antibody, a monoclonal antibody, a recombinant antibody, a humanised antibody, a human antibody and a fragment thereof.

8. The probe of claim 7, in which the antibody is directed against an epitope of each receptor located in an extracellular domain adjacent to a site for binding ATP.

9. The probe of claim 1, wherein the receptors are mammalian $P2X_7$ receptors and the probe is adapted to distinguish between functional receptors having a sequence in which proline at amino acid 210 is in the trans conformation and non-functional receptors having a sequence in which the proline at amino acid 210 is in the cis conformation acting to alter local protein structure.

10.   The probe of claim 1, wherein the receptors are mammalian $P2X_7$ receptors and the probe is adapted to distinguish between functional receptors having a sequence in which proline at amino acid 199 is in the trans conformation and non-functional receptors having a sequence in which the proline at amino acid 199 is in the cis conformation acting to alter local protein structure.

11.   The probe of claim 9, wherein the probe is or includes an antibody raised against an epitope sequence of the $P2X_7$ receptor extending from Gly200 to Cys216.

12.   The probe of claim 9, wherein the probe is or includes an antibody raised against an epitope sequence of the $P2X_7$ receptor extending from Gly200 to Thr215.

13.   The probe of claim 1, wherein the probe is an antibody that specifically binds to an epitope within residues Gly200 to Cys216 of a $P2X_7$ receptor without specifically binding to other regions of the P2X7 receptor.

14.   The probe of claim 1, wherein the disease or condition is chosen from the group consisting of: prostate, breast, skin, lung, cervix, uterus, stomach, oesophagus, bladder, colon and vaginal cancers, other epithelial cell cancers, malignant lymphoma, other blood cancers, irritable bowel syndrome and infection by a virus or other pathological organism.

15.   The probe of claim 14, wherein the virus or organism is HIV or Mycobacterium tuberculosis.

16.   The probe of claim 7, wherein the condition is irritable bowel syndrome and the antibody is capable of detecting other regions of the $P2X_7$ receptor unchanged by functional state by detecting an epitope common to both functional and non-functional conformations.

17.   The probe of claim 7, wherein the condition is irritable bowel syndrome and the antibody is used in combination with a second antibody capable of detecting total $P2X_7$ expression. A probe that specifically binds an epitope outside residues Gly200 to Cys216 of a $P2X_7$ receptor without specifically binding to an epitope within Gly200 to Cys216 of the $P2X_7$ receptor.

18.   A method for detecting a disease or condition, the method including the steps of:

using the probe of claim 1 to distinguish between functional $P2X_7$

receptors and non-functional $P2X_7$ receptors,

providing a receptor expression profile, and

comparing the receptor expression profile with that of a normal profile.

19.   The method of claim 18, wherein the receptor expression profile is a proportion of non-functional $P2X_7$ receptors to total $P2X_7$ receptors, and a higher proportion of non-functional receptors to total $P2X_7$ receptors in the receptor expression profile relative to the normal profile indicates presence of the disease or condition.

20.   The method of claim 18, wherein the receptor expression profile is that of non-functional receptors.

21.   The method of claim 18, wherein the probe is adapted to distinguish between functional $P2X_7$ receptors and non-functional $P2X_7$ receptors by detecting change in relation to binding of adenosine triphosphate (ATP) to the receptors.

22.   The method of claim 18, wherein the probe is adapted to distinguish between functional $P2X_7$ receptors and non-functional $P2X_7$ receptors by detecting change in binding of one or more proteins necessary for pore formation in $P2X_7$ receptors.

23.   The method of claim 18, wherein the probe is adapted to distinguish between functional $P2X_7$ receptors and non-functional $P2X_7$ receptors by detecting one or more parts of the receptor exposed in the absence of bound ATP.

24.   The method of claim 23, wherein the part includes a $P2X_7$ monomer.

25.   The method of claim 18, wherein the receptor expression profile is provided using *in situ* imaging techniques.

26.   The method of claim 18, wherein the receptor expression profile is provided using microscopy, confocal microscopy or fluorescence activated cell sorting.

27.   An isolated cell or tissue sample complexed with a probe as claimed claims 1.

28.   A method of diagnosing irritable bowel syndrome, comprising detecting the P2X$_7$ expression profile of cells and/or tissue and comparing the profile with a predetermined expression profile of normal cells and/or tissue.

29.   The method of claim 28, wherein the cells and/or tissues are intestinal cells or tissue.

30.   The method of claim 28, wherein the detection of the P2X$_7$ expression profile includes use of one or more antibodies.

31.   A method of treating irritable bowel syndrome, the method including administering a composition adapted to restore P2X$_7$ receptor function.

32.   An antibody being adapted to distinguish between functional P2X$_7$ receptors and non-functional P2X$_7$ receptors and to bind only to non-functional receptors.

33.   The antibody of claim 32, wherein the antibody is adapted to distinguish between functional P2X$_7$ receptors and non-functional P2X$_7$ receptors by detecting change in relation to binding of adenosine triphosphate (ATP) to the receptors.

34.   The antibody of claim 32, wherein the antibody is adapted to distinguish between functional P2X$_7$ receptors and non-functional P2X$_7$ receptors by detecting change in binding of one or more proteins necessary for pore formation in P2X$_7$ receptors.

35.   The antibody of claim 32, wherein the antibody is adapted to distinguish between functional P2X$_7$ receptors and non-functional P2X$_7$ receptors by detecting one or more parts of the receptor exposed in the absence of bound ATP.

36.   The antibody of claim 35, wherein the part includes a P2X$_7$ monomer.

37.   The antibody of 32, which is polyclonal, monoclonal, recombinant, humanised or a human antibody or an appropriate fragment thereof.

38.   The antibody of claim 32, wherein the receptors are mammalian P2X$_7$ receptors and the antibody is adapted to distinguish between functional receptors having a sequence in which proline at amino acid 210 is in the trans conformation and non-functional

receptors having a sequence in which the proline at amino acid 210 is in the cis conformation.

39.   The antibody of claim 38, which is raised against an epitope sequence of the $P2X_7$ receptor extending from Gly200 to Cys216.

40.   The antibody of claim 39, which is raised against an epitope sequence of the $P2X_7$ receptor extending from Gly200 to Thr215.

41.   The antibody of claim 32, wherein the receptors are mammalian $P2X_7$ receptors and the antibody is adapted to distinguish between functional receptors having a sequence in which proline at amino acid 199 is in the trans conformation and non-functional receptors having a sequence in which the proline at amino acid 199 is in the cis conformation

42.   The antibody of claim 32, wherein the disease or condition is chosen from the group consisting of: prostate, breast, skin, lung, cervix, uterus, stomach, oesophagus, bladder, colon and vaginal cancers, other epithelial cell cancers, malignant lymphoma, other blood cancers, irritable bowel syndrome and infection by a virus or other pathological organism.

43.   The antibody of claim 42, wherein the virus or organism is HIV or Mycobacterium tuberculosis.

44.   An epitope adapted to cause the generation of the antibody of claim 32.

45.   The epitope of claim 44, which is attached to diphtheria toxin via the C-terminal Cys residue by means of the chemical cross-linker maleimidocaproyl-N-hydroxysuccinimide (MCS), so that the conformation adopted by the attached epitope peptide occupies a stable cis proline configuration.

46.   An isolated polypeptide comprising a segment of a $P2X_7$ receptor of up to 30 amino acids including Gly200 to Cys216.

47.   The isolated polypeptide of claim 46, wherein the segment consists of Gly200 to Cys216.

48.   An isolated polypeptide comprising a segment of a $P2X_7$ receptor of up to 30 contiguous amino acids including Gly200 to Thr 215.

49.   The isolated polypeptide of claim 48, consisting of Gly200 to Thr215.

50.   A pharmaceutical composition for treatment or prevention of a disease or condition in a patient, the composition including a pharmaceutically effective amount of an antibody as claimed in claim 32, or an epitope to cause the generation of such an amount, capable of regulating programmed cell death of cells having expressed on their surface aberrant or non-functional $P2X_7$ receptors.

51.   A preparation for treatment or prevention of a disease or condition in a patient, the preparation including one or more substances adapted to regulate the expression of ATPases or ATPDases that control the supply of ATP to $P2X_7$ receptors in the patient's cells or tissues.

52.   A method of treating or preventing a disease or condition in a patient, the method including the step of administering to the patient a preparation including one or more substances adapted to regulate the expression of ATPases or ATPDases that control the supply of ATP to $P2X_7$ receptors in the cells or tissue of the patient.

53.   The preparation of claim 51, wherein the disease or condition is chosen from the group consisting of: prostate, breast, skin, lung, cervix, uterus, stomach, oesophagus, bladder, colon and vaginal cancers, other epithelial cell cancers, malignant lymphoma, other blood cancers, irritable bowel syndrome and infection by a virus or other pathological organism.

54.   The method of claim 52, wherein the disease or condition is chosen from the group consisting of: prostate, breast, skin, lung, cervix, uterus, stomach, oesophagus, bladder, colon and vaginal cancers, other epithelial cell cancers, malignant lymphoma, other blood cancers, irritable bowel syndrome and infection by a virus or other pathological organism.

55.   The antibody of claims 32, wherein the antibody is a chimeric, humanized or human antibody or fragment thereof.

56. The antibody of claim 55, when combined with a radiolabel suitable for detection by use of scanning technology.

57. The antibody of claim 55, when the scanning technology is positron emission tomography.

58. The antibody of claim 56, when combined with a fluorescent label suitable for use in flow cytometry.

59. The antibody of claim 56, when combined with a matrix suitable for colorimetric assay.

60. A test kit for detecting non-functional $P2X_7$ receptors, the kit including the probe of claim 1 , together with a normal $P2X_7$ receptor expression profile.

61. A test kit for detecting non-functional $P2X_7$ receptors, the kit including the antibody of claim 32, together with a normal $P2X_7$ receptor expression profile.

62. A test kit for detecting non-functional $P2X_7$ receptors, the kit including the antibody of claim 56, together with a normal $P2X_7$ receptor expression profile.

63. The test kit of claim 60, when adapted to detect non-functional $P2X_7$ receptors in a blood sample.

64. A diagnostic kit comprising:(1) a probe that that specifically binds to an epitope within residues Gly200 to Cys216 of a $P2X_7$ receptor without specifically binding to other regions of the $P2X_7$ receptor, and (2) a probe that specifically binds an epitope outside residues Gly200 to Cys216 of a $P2X_7$ receptor without specifically binding to an epitope Gly200 to Cys216 of the $P2X_7$ receptor.

65. The preparation of claim 51, in which the ATPases and ATPDases are chosen from CD39 and CD73.

66. The preparation of claim 51, wherein the one or more substances is one or more ATP analogues.

67.   A method of treating or preventing a disease or condition, the method including use of the antibody claimed in claim 32.

68.   A method of treating or preventing a disease or condition, the method including use of the epitope of claim 44.

69.   A method of treating or preventing a disease or condition, the method including use of the pharmaceutical composition of claim 50.

70.   A method of treating or preventing a disease or condition, the method including use of the preparation of claim 51.

71.   The probe of claim 16, wherein the epitope is Val65-Lys81.